UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trad mark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/449,631	11/30/99	RENNER	W 1700.0030002

EXAMINER	
MOSHER, M	
ART UNIT	PAPER NUMBER
1648	15

DATE MAILED: 06/06/01

HM22/0606
STERNE KESSLER GOLDSTEIN & FOX PLLC
SUITE 600
1100 NEW YORK AVENUE NW
WASHINGTON DC 20005-3934

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/449,631	Renner t al
Examiner	**Art Unit**
Mary Mosher	1648

-- Th MAILING DATE of this communication appears n the cover sheet with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *3/22/01*

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-49* is/are pending in the applica

4a) Of the above, claim(s) *5-7, 9, 13-16, 19-23, 31, 32, and 47-49* is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-4, 8, 10-12, 17, 18, 24-30, and 33-46* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirem

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *14, 10, 8*

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

Election/Restriction

Applicant's election of species hepatitis B core, leucine zipper attachment, bee sting allergy antigen in Paper No. 13 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 5-7, 9, 13-16, 19-23, 31, 32, 47-49 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 13.

Therefore claims 1-4, 8, 10-12, 17, 18, 24-30, 33-46 have been examined.

The elected species, hepatitis core particle, leucine zipper organizer/attachment, and honeybee allergen, is free of the art. Search has therefore been extended to determine if the genus described in claim 1 is allowable.

Claim Objections

Claim 36 objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 35 is directed to a method of immunization. Claim 36 states that the immunization produces an immune response. If no immune response is produced, the

immunization method is obviously inoperative. Therefore there is no difference in scope between claims 35 and 36, because claim 35 is assumed to exclude obviously inoperative embodiments.

Claim Rejections - 35 USC § 112

Claims 1-4, 8, 10-12, 17, 18, 24-30, and 33-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 uses the terms ""core particle", "organizer", and "attachment site" as some key elements in describing the invention. To understand the metes and bounds of the claimed invention, the specification is consulted for its definition of these terms. Pages 10-17 contain definitions of terms; pages 12, 15, and 11-12 are particularly relevant in defining these terms. As defined in the specification, the "core particle" has a rigid structure with an inherent repetitive organization. This is reasonably clear. The "organizer" is an element bound to a core particle in non-random fashion, that provides a nucleation site for creating an ordered and repetitive antigen array. The "organizer" may be a polypeptide, an amino acid residue within a polypeptide, a sugar, a polynucleotide, a polymer, a metal ion or chemical compound, a combination of these materials, or a chemically reactive group of any of these materials. The "organizer" must contain a first attachment site. The list of possible materials for an attachment site is identical to the list of materials for an organizer. The second attachment site is associated with an antigen, and it associates with the first attachment site through any mechanism except a peptide bond.

The meaning of "organizer" is confusing, particularly in light of the working examples. See examples 23-25, for instance. HBV cAg forms the core particle and FLAG is the antigen. cAg and FLAG are connected by a linker SPDP, which covalently links FLAG to an engineered His residue in cAg. What is the "organizer" in this example? The only nucleation site for forming a repetitive array is somewhere within the structure of the cAg, but cAg forms the core particle, and a core particle is an element separate from the organizer in the claim. The engineered histidine residue might be the first attachment site, but it is not involved in nucleation, because the particle can assemble without the histidine residue. So it is not at all clear what constitutes the "organizer" in this working example. Without a clear understanding of the metes and bounds of an "organizer" as used in the claim, the metes and bounds of the invention are indefinite.

Does the broad invention involve an antigen (or hapten) which is covalently or noncovalently bound to a structured core particle, the antigen is presented on the surface of the particle in some regular, ordered spacing, and fusion proteins (where the antigen forms a continuous polypeptide with the core subunit) are excluded? This seems to be what the invention is about, but this is not what the claims define. In the interest of compact prosecution, the claims have been examined as if the "organizer" and the two "attachment sites" collectively meant anything connecting the antigen to the core particle, as long as the antigen was not fused to core particle subunits as a single continuous polypeptide. However, this treatment does not relieve applicant of the burden of response to this rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1, 24, 27, and 41 are rejected under 35 U.S.C. 102(B) as being anticipated by Quash et al (Journal of immunological methods 1978, 22 (1-2) p165-74, abstract only cited). In Quash et al, the latex particle is a core particle of non-natural origin, the side arm is the organizer, the primary amine and hydrazine groups are the first attachment site, the glycoproteins are the antigen, and the artificially-generated aldehyde groups on the antigen are the second attachment site which associates with the first attachment site through a non-peptide bond. Therefore the reference meets each and every limitation for these claims.

Claims 1, 24, 27, and 41 are rejected under 35 U.S.C. 102(b) as being anticipated by Ikram et al (Journal of virological methods 1981, 2 (5) p269-75). In Ikram et al, the erythrocyte is a core particle of natural origin, the organizer/1st attachment site is a chemically reactive group on the erythrocyte, the 2nd attachment site is a chemically reactive group on HbSag, and the 1st and 2nd attachment sites associate through a non-peptide chemical coupling. Therefore the reference meets each and every limitation for these claims.

Claims 1-4, 24, 25, 27-30, 34, 41, 43, and 44 are rejected under 35 U.S.C. 102(b) as being anticipated by Watkins et al (Gene therapy Oct 1997, 4 (10) p1004-12, abstract only cited). In this reference, the adenovirus is the core particle, the organizer comprising the first attachment site is an antigenic part of the adenovirus fiber protein, EGF is the antigen, and the scFv antibody (fused to EGF) is the second attachment site. Therefore the reference meets each and every limitation for these claims.

Claims 1, 24, 25, 27, 33-37, 40-42 are rejected under 35 U.S.C. 102(b) as being anticipated by Hunter (EP 0 283 505). In this reference, polymerized flagellin is the core particle, an amino acid residue in flagellin is the first attachment site, and the antigen associates with the first attachment site by the chemical cross-linker. The reference also explicitly teaches vaccines and administration of the conjugates. Therefore the reference meets each and every limitation for these claims.

Claims 1, 24, 25, 27, 33-41 are rejected under 35 U.S.C. 102(e) as being anticipated by Rock (US 5,928,647). In this reference, iron oxide, silica, or polystyrene is the core particle, a reactive group in the core is the first attachment site, and the antigen associates with the first attachment site by the chemical cross-linker. Therefore the reference meets each and every limitation for these claims.

Claims 1-4, 24, 27-30, 33-35, 41, 43, and 44 are rejected under 35 U.S.C. 102(e) as being anticipated by Larocca et al (US 6,054,312). In this reference, a bacteriophage is the core particle, and a ligand is attached to the core by avidin/biotin linkage (col. 23) or chemical cross-linking

(col.24) or other linking methods (col. 25). Although the reference does not state that the attached ligands are antigens, the ligands necessarily and inherently are antigens (as defined by applicant), since the ligands discussed in the reference are capable of being bound by an antibody. The reference also teaches administration. Therefore the reference meets each and every limitation for these claims.

Information Disclosure Statement

The Information Disclosure Statement filed 4/14/2000 has not been considered yet, because the references were either separated from the file and lost, or not provided. The references will be considered at a future date. Would it be possible to provide replacement copies of the references? Please contact the Examiner to arrange the details to try to avoid losing the references again; replacement copies provided at about the same time as the next response would be appreciated.

Allowable Subject Matter

Claims 8, 10-12, 17, 18, 26, 45, and 46 appear to be free of the art, for the following reasons. The prior art teaches fusion of antigen sequences to proteins forming virus-like particles or capsid particles, but does not appear to teach or suggest attachment of antigens to a virus-like particle in a repetitive pattern through a linkage that does not involve fusion to a subunit assembling in the particle. Similarly, the prior art does not teach such linkage to proteins of the viruses recited in claim 17, or using a leucine zipper to link antigens to a core particle.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary E. Mosher, Ph.D. whose telephone number is (703) 308-2926. The examiner can normally be reached on Monday -Thursday and alternate Fridays from 6:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (703) 308-4027. The fax phone number for this Group is now (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

June 4, 2001

MARY E. MOSHER
PRIMARY EXAMINER
GROUP 1800

1600